REMARKS

Initially it should be noted that in the March 28, 2003 Office Action, the Office rejected the then pending claim 4, as shown below, as not meeting the enablement requirements under 35 USC §112, first paragraph.

> 4. The composition according to claim 3, characterized in that the antibody is the monoclonal anti-CD66a 4D1/C2 antibody which was deposited with DSMZ (German-Type Collection of Microorganisms and Cell Cultures) Braunschweig under DSM ACC2371 on October 22, 1998.

The Office stated in the March 28, 2003 Office Action that;

> "Claim 4 is rejected under 35 USC §112, first paragraph because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention, because the specification does not provide evidence that the claimed biological materials are 1) known and readily available to the public; (2) reproducible from the written description. . . . **Therefore it would require undue experimentation to reproduce the claimed antibody species 4D1/C2. Deposit of the hybridoma would satisfy the enablement requirement of 35 USC §112, first paragraph.** See 37 CFR 1.801-1.809." (emphasis added))

In response to the March 28, 2003 Office Action, applicants cancelled claim 4 and incorporated the subject matter relating to the deposited antibody into claim 1. Further, on November 21, 2003, applicants submitted a Declaration attesting to the deposit of the biological material.

On December 5, 2003 the Office issued a final rejection of the claims. Also, because the Declaration that was submitted on November 21, 2003 had not yet been matched with the prosecution file at the PTO, the Office rejected amended claims 1, 2, 6 and newly added claim 8 for lack of enablement. Specifically the Office stated that:

> "The rejection of newly amended claims 1-2, 6, and 8 under 35 USC §112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention, because the specification does not provide evidence that the claimed biological materials are (1) know and readily available to the public; (2) reproducible from the written description is maintained.

> The response filed 9/18/03 has been carefully considered but is deemed not to be persuasive. The response states Applicants have requested a copy of the Certificate of the Availability, but to date have not received it (see page 5 of response). In response to this argument, all assurances have not been met and as such the rejection stands."

Thus, it was evident that the Office maintained the lack of enablement requirement because applicants' Declaration, which provided proof of deposit of the claimed monoclonal antibody, had not yet been matched with the prosecution file of the present application.

Applicants filed a response to the December 5, 2003 Final Office Action on February 24, 2004 and the Office issued an Advisory Action on March 2, 2004 refusing to enter the newly amended claims submitted on February 24, 2004 because according to the Office the amendment of claims required a further search. In response, applicants filed a RCE on May 19, 2004 to force the entry of the February 24, 2004 amendment.

October 28, 2004 Office Action

In the October 28, 2004 Office Action, the Office withdrew the rejection of claims 1-2, 6 and 8 under 35 USC §112, first paragraph for lack of enablement because the Office had finally received the declaration that applicants filed on 11/21/03 and provided proof that the deposit requirement had been completed.

Additionally, the Office maintained the rejection of claims 1, 2, 6 and 8 under 35 U.S.C. §102(b) as being anticipated by Drzeniek, et al. (Cancer Letters, 56: 173-179, 1991) or Prall, et al. (The Journal of Histochemistry and Cytochemistry 44: 35-41, 1996).

Claim 1 recites as follows:

> 1. A pharmaceutical composition for reducing angiogenesis in tumor cells, the method comprising
>
> monoclonal anti-CD66a antibody which was deposited with DSMZ (German-Type Collection of Microorganisms and Cell Cultures) Braunschweig under DSM ACC2371 on October 22, 1998 and a pharmaceutically compatible carrier, wherein the monoclonal anti-CD66a antibody is in a therapeutically

active amount to reduce formation of capillaries in the tumor cells by functionally blocking CD66a on tumor endothelial cell.

Thus, claim 1 includes:

1. a monoclonal anti-CD66a antibody which was deposited with DSMZ (German-Type Collection of Microorganisms and Cell Cultures) Braunschweig under DSM ACC2371 on October 22, 1998;

2. a pharmaceutically compatible carrier; and

3. the monoclonal anti-CD66a antibody is in a therapeutically active amount to reduce formation of capillaries in the tumor cells by functionally blocking CD66a on tumor endothelial cell.

According to the Office this claim 1 meets all enablement requirements under 35 USC §112, first paragraph because the monoclonal antibody was deposited. This act of depositing the antibody enables any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention. Without this proof of depositing the presently claimed monoclonal antibody, the Office stated that the specification did not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from the written description.

To anticipate a claim, a reference must be enabling. This point was recently reaffirmed in an April 7, 2000 decision of the Court of Appeals for the Federal Circuit (CAFC).[1] Citing *In re Paulsen*,[2] the court stated that to be anticipating, a prior art reference must:

1) disclose each and every limitation of the claimed invention;

2) be enabling; and

3) describe the claimed invention sufficiently to place it in possession of a person of ordinary skill in the field of the invention.

Neither Drzeniek, et al. nor Prall, et al. meets this standard.

[1] *Helifix Ltd. v. Blok-Lok, Ltd.*, 54 USPQ2d 1299 (Fed. Cir. 2000).
[2] *In re Paulsen*, 31 U.S.P.Q.2d 1671, 1673 (Fed. Cir. 1994).

According to the Office, the claimed antibodies are disclosed in the Drzeniek, et al. and Prall, et al. references. Applicants vigorously disagree. The Office has the initial burden of establishing a *prima facie* case of anticipation by pointing out where all the claim limitations appear in a single reference. *In re Spada* 15 USPQ2d 1655 (Fed. Cir. 1990). Thus the Office has to show in each cited reference the following limitations;

1. a monoclonal anti-CD66a antibody which was deposited with DSMZ (German-Type Collection of Microorganisms and Cell Cultures) Braunschweig under DSM ACC2371 on October 22, 1998;

2. a pharmaceutically compatible carrier; and

3. the monoclonal anti-CD66a antibody is in a therapeutically active amount to reduce formation of capillaries in the tumor cells by functionally blocking CD66a on tumor endothelial cell.

The Office has not carried the required burden of establishing a *prima facie* case of anticipation because the Office has not indicated in each reference these limitations.

Further, it is clear that neither of these references is enabling and/or describes the claimed invention sufficiently to place it in possession of a person of ordinary skill in the field of the invention. Applicants' claims and specification were rejected for lack of enablement until the Office received proof that the monoclonal antibody was deposited because according to the Office the present specification did not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention, because the specification does not provide evidence that the claimed biological materials are (1) known and readily available to the public; (2) reproducible from the written description.

Applicants submit that this same lack of enablement is also applicable to the descriptions set forth in both of the cited references. Neither of the references provides a sufficient description or guidance to reproduce the antibodies discussed therein. Clearly, the descriptions in the references are not enabling because the monoclonal antibodies discussed therein cannot be reproduced from the descriptions of either reference.

According to the Office, applicants admit that the antibody in the specification is the same as that disclosed in the references. In response, applicants submit that this statement in the specification does not provide any information on the antibodies discussed in the cited references and further

this statement by applicants certainly was not considered by the Office to be sufficient to overcome the section 112, first paragraph rejections. Instead, applicants to show enablement, had to provide proof that the presently claimed monoclonal antibody was deposited. Clearly, the cited references do not provide sufficient enablement for one skilled in the art to practice the present invention, because the present invention comprises a deposited antibody that was not deposited at the time of the cited references.

Further, this hypothetical admission by applicants still did not convince the Office that the present description was enabling or that the present specification provided evidence that the biological materials were available to the public. Instead, the Office stated that:

> "the present specification did not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention, because the specification does not provide evidence that the claimed biological materials are (1) **known and readily available to the public**; (2) reproducible from the written description." (emphasis added)

The Office cannot have it both ways. If applicants have not met the enabling requirements due to the lack of proof of depositing the claimed monoclonal, the mere mention of some antibodies in the cited references certainly **cannot** be considered as enabling disclosures.

As applicants stressed in a previous response, neither reference clearly shows that the described antibodies in the respective references are the same when compared to each other or whether the disclosed antibodies are the same as the presently claimed antibody. Drzeniek, et al, discusses three specific antigens having a molecular weight of 85,000; 115,000 or 170,000. The Drzeniek, et al, reference clearly stated that the discussed MAb 4D1/C2 antibody binds preferentially to the antigen of M_r 85,000. It should be noted that there was no binding to an antigen of M_r 170,000 (see page 177, top of column 2). In contrast, the MAb 4D1/C2 discussed in the Prall, et al. reference binds to an antigen having a M_r of 160,000. It is apparent that the two cited references disclose two separate and distinct monoclonal antibodies that may have the same name but certainly do not bind to the same antigen.

Furthermore, are the Drzeniek, et al., and Prall, et al. references so clear and explicit that one skilled in the art will have no difficulty in ascertaining what is disclosed? Applicants contend that the references **are not clear and explicit**, in fact, the exact binding of the discussed antibodies to

which antigen is uncertain because of the ambiguous and seemingly contradictory statements in the Drzeniek, et al. and Prall, et al. references.

Applicants question as to which one of the cited reference is anticipatory. Each reference is vague and uncertain to such an extent as to beg the question of whether either reference is enabling because of the fundamental ambiguities that are introduced when comparing the two references. It is well established as a matter of law that before a reference can be prior art under section 102, a reference **must be enabling and it must put the claimed invention in the hands of one skilled in the art.** (*In re Sun*, 31 USPQ2d 1451 (Fed. Cir. 1993)). At this point, applicants submit that neither reference puts the claimed invention in the hand of one skilled in the art.

In response to the Office's contention that Drzeniek, et al. and Prall, et al. describe antibodies that would inherently reduce angiogenesis and reduce formation of capillaries, applicants submit that it is well settled as a matter of law, that inherency cannot be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient to establish inherency. *In re Oelrich*, 212 USPQ 323 (CCPA 1981). Instead, it must consistently occur each and every time, which is necessary under case law to prove inherency.

Drzeniek, et al. describes binding to a glycoprotein isolated from human bile and there is no discussion that this glycoprotein was expressed by human endothelial cells. The Prall, et al. reference discusses the use of "unknown" antibodies that bind to specific groups on granulocytes and this binding reduces angiogenesis, however, the reference is completely silent on using the presently claimed antibody for reducing angiogenesis in tumor endothelial cells. Thus, the systems set up in both references could not possible cause the reduction of capillary growth in tumors. Moreover, neither reference is enabling to provide guidance to one skilled in the art to go in the direction of applicants' claimed invention.

Accordingly, applicants respectfully submit that the pending claims are patentably distinguishable over Drzeniek, et al. and Prall, et al. Withdrawal of this rejection under 35 U.S.C. §102(b) is requested.

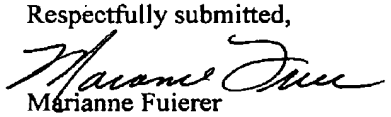
Fee Payable and Petition for Extension of Time.

Applicants hereby petitions for a three (3) month extension of time, extending the deadline for responding to the July 28, 2004 2003 Office Action from October 28, 2004 to January 28, 2005. The entry of this petition results in a petition fee of $510.00. A credit card authorization form in the amount of $510.00 is included herein for payment of the petition fee. The U.S. Patent and Trademark Office is hereby authorized to charge any additional amount necessary to the entry of this amendment, and to credit any excess payment, to Deposit Account No. 08-3284 of Intellectual Property/Technology Law.

Conclusion

Applicants have satisfied the requirements for patentability. All pending claims are free of the art and fully comply with the requirements of 35 U.S.C. §112. It therefore is requested that Examiner Helms reconsider the patentability of pending claims in light of the distinguishing remarks herein and withdraw all rejections, thereby placing the application in condition for allowance. Notice of the same is earnestly solicited. In the event that any issues remain, Examiner Helms is requested to contact the undersigned attorney at (919) 419-9350 to resolve same.

Respectfully submitted,



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